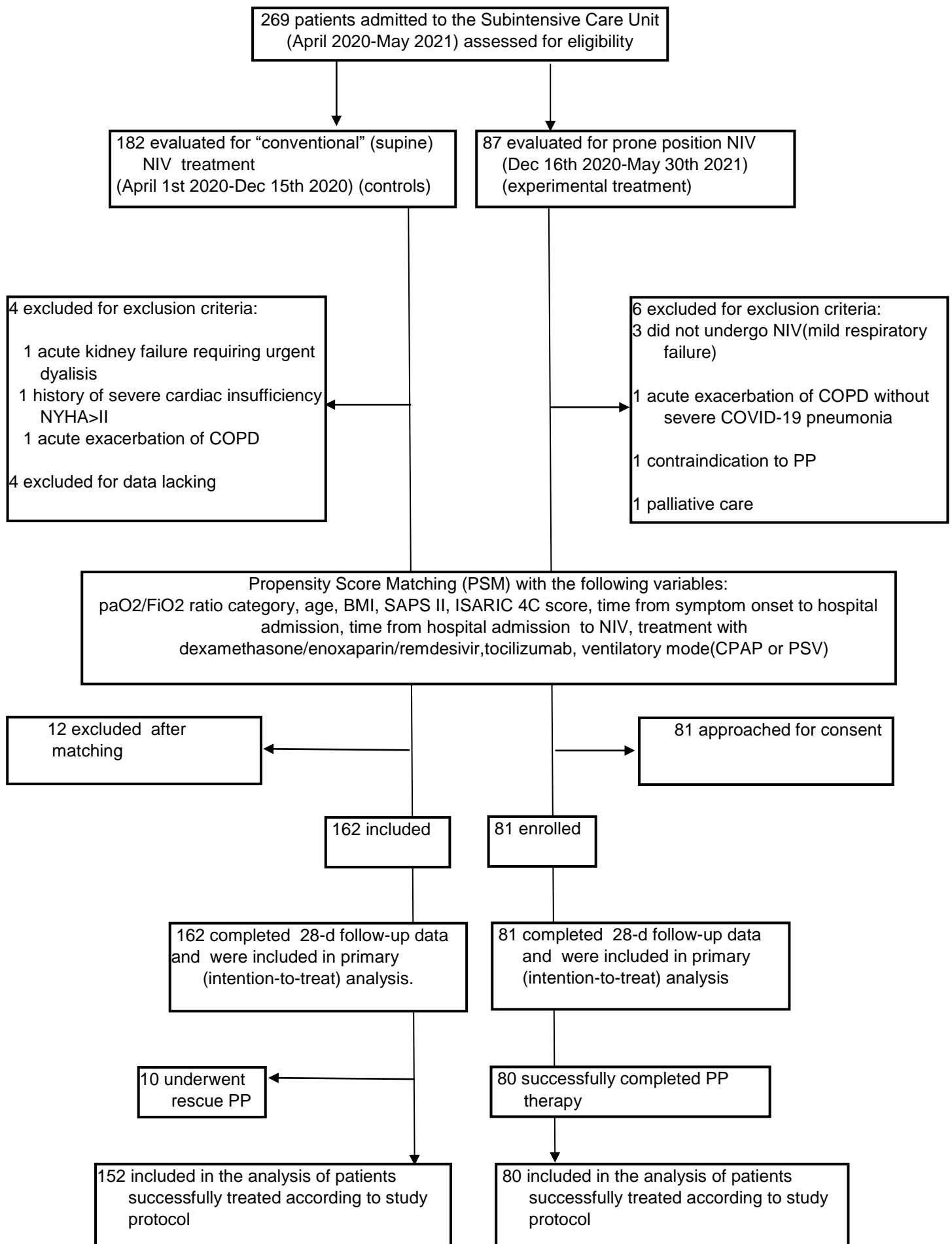


Supplementary Figures

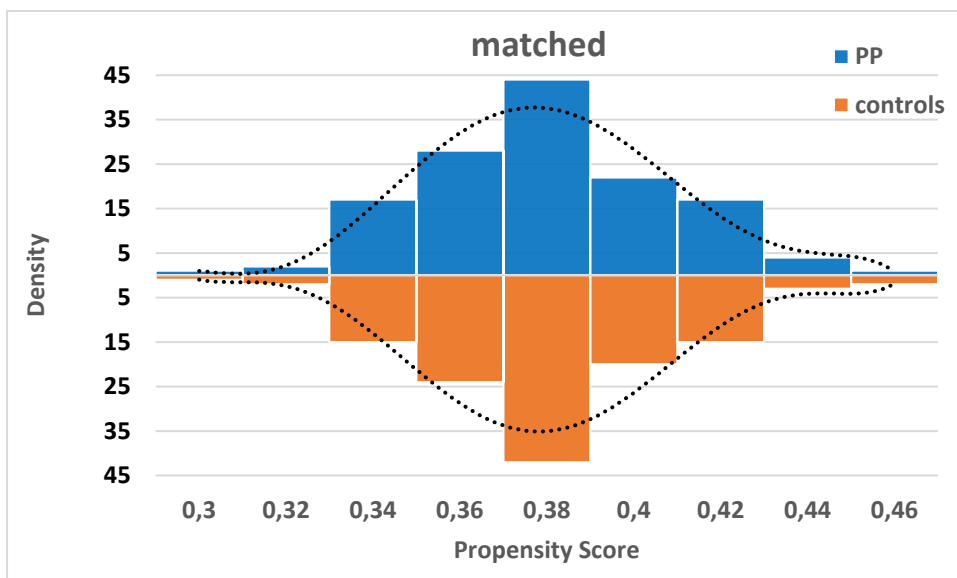
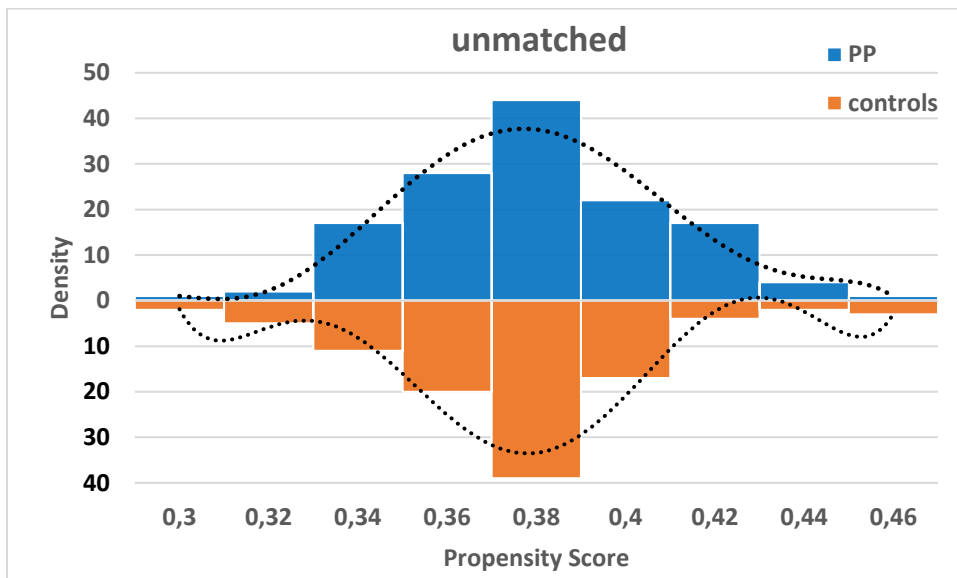
Early prolonged prone position in noninvasively ventilated patients with SARS-CoV-2-related moderate-to-severe hypoxemic respiratory failure: clinical outcomes and mechanisms for treatment response in the PRO-NIV study

Supplementary Figure 1: flow of participants through study

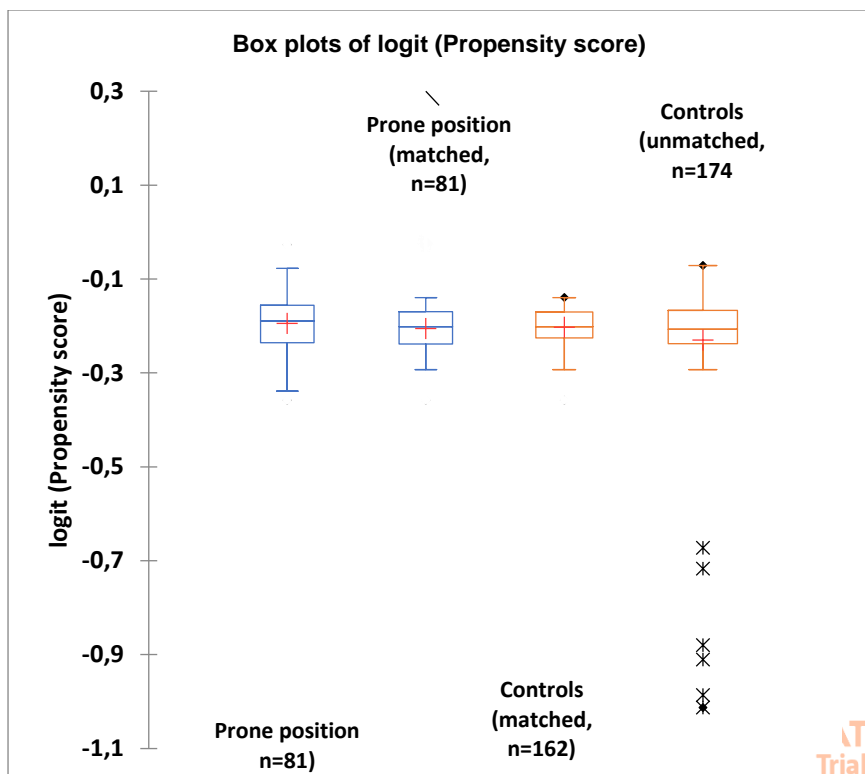


Supplementary Figure 2. Propensity score(PS) density in PP and controls before and after matching (panel A) and balance plots of logit(PS) in PP and controls before and after matching(panel B)

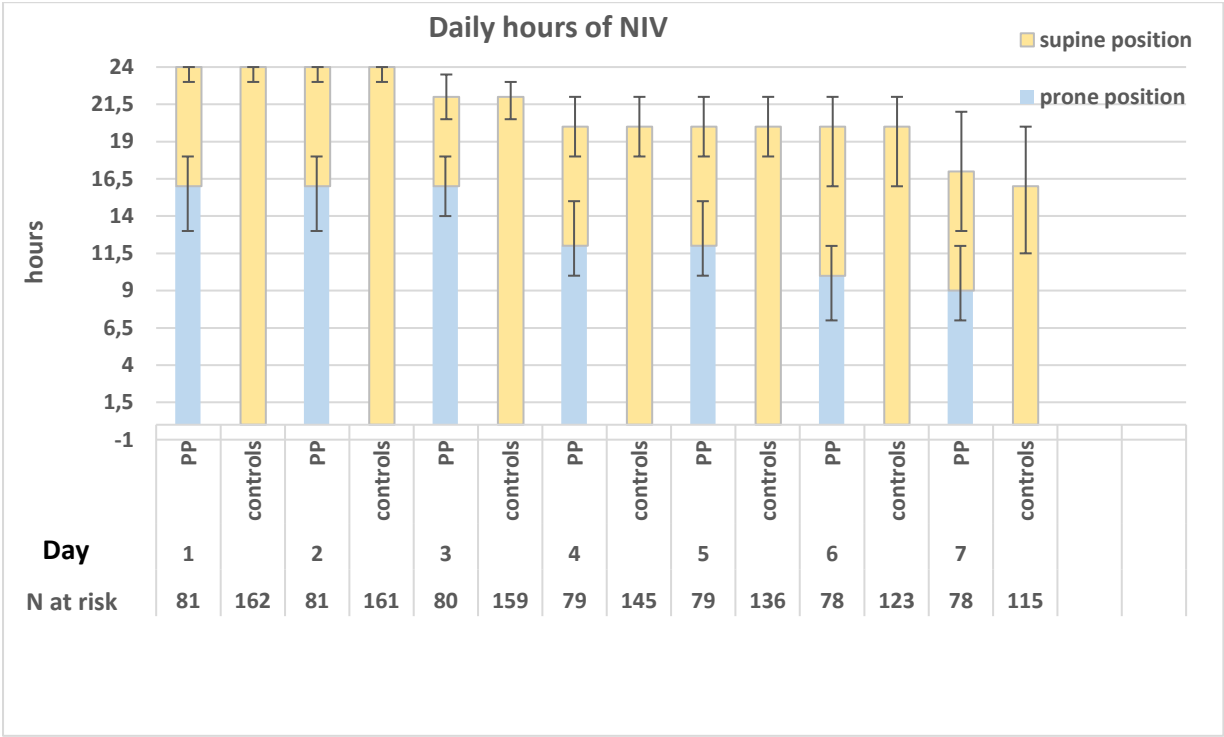
Panel A: Propensity Score Distribution before and after matching



Panel B: balance plots of logit (Propensity Score) in PP and controls before and after matching

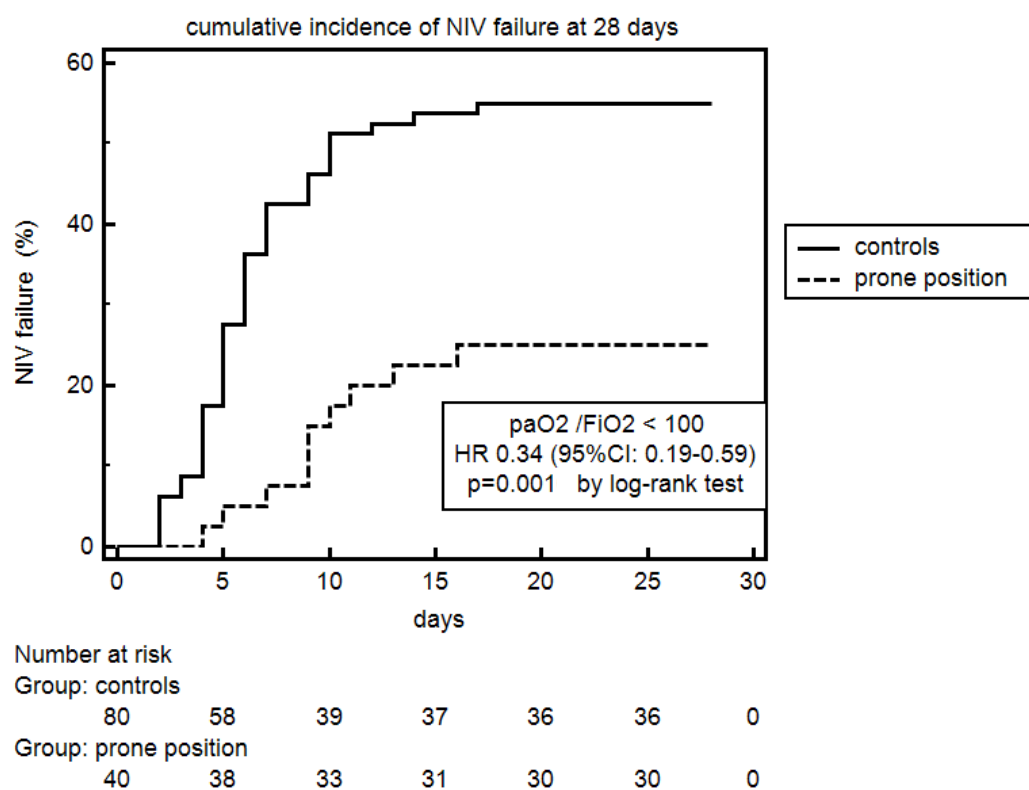


Supplementary Figure 3. Total daily hours of NIV and of NIV in prone position in both groups during the initial 7 study days in the whole study populaton (n=243). Bars represent the median, whiskers the IQR1 and IQR3

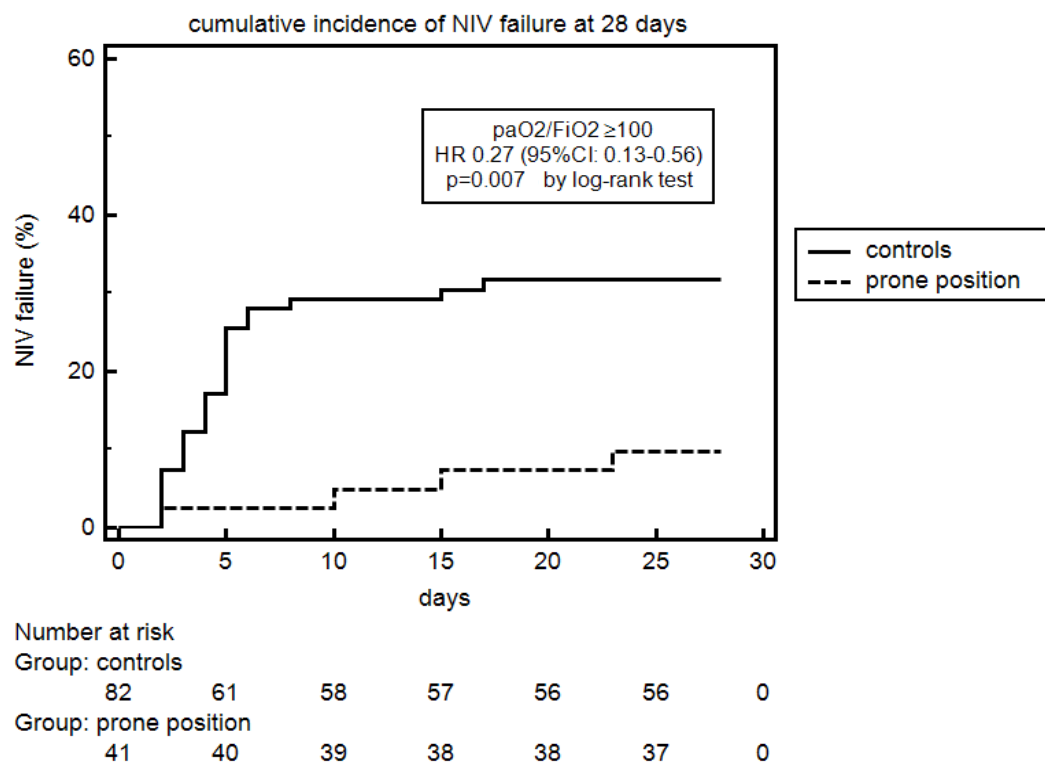


Supplementary Figure 4. NIV failure, death and endotracheal intubation in patients grouped according to $\text{paO}_2/\text{FiO}_2$ at admission: $\text{paO}_2/\text{FiO}_2 < 100$ vs $\text{paO}_2/\text{FiO}_2 100-199$

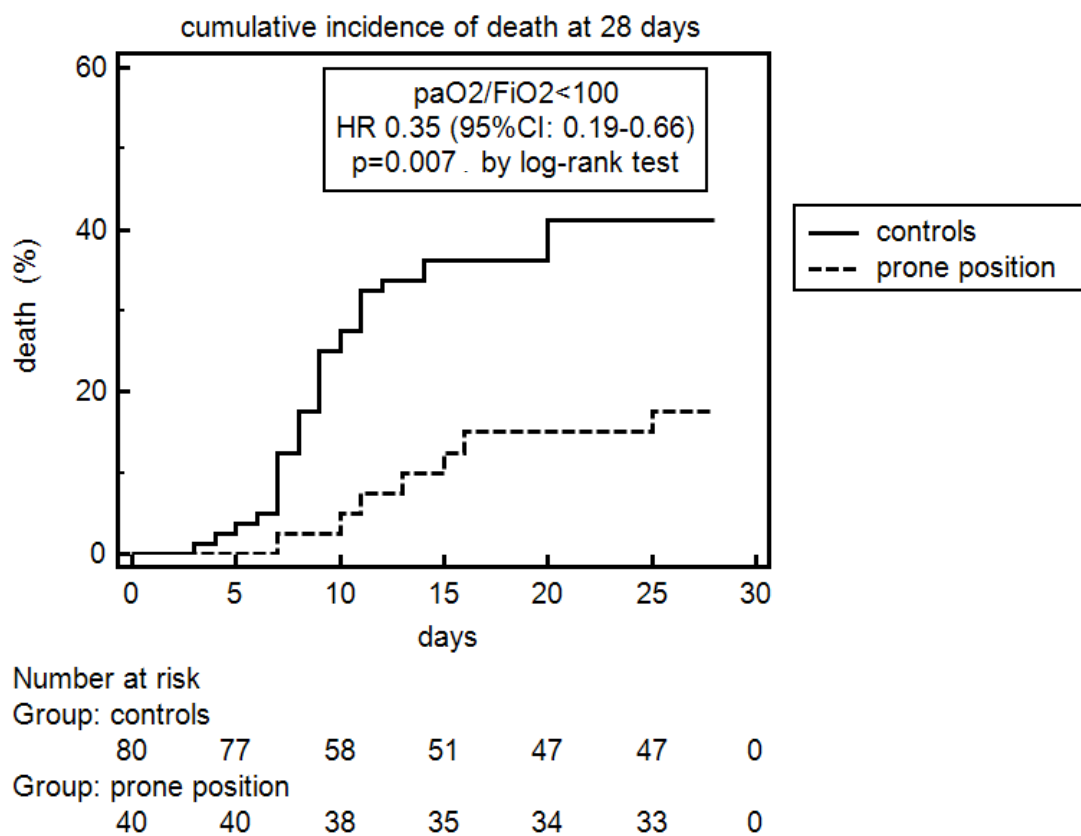
Panel A: NIV failure in patients with $\text{paO}_2/\text{FiO}_2 < 100$



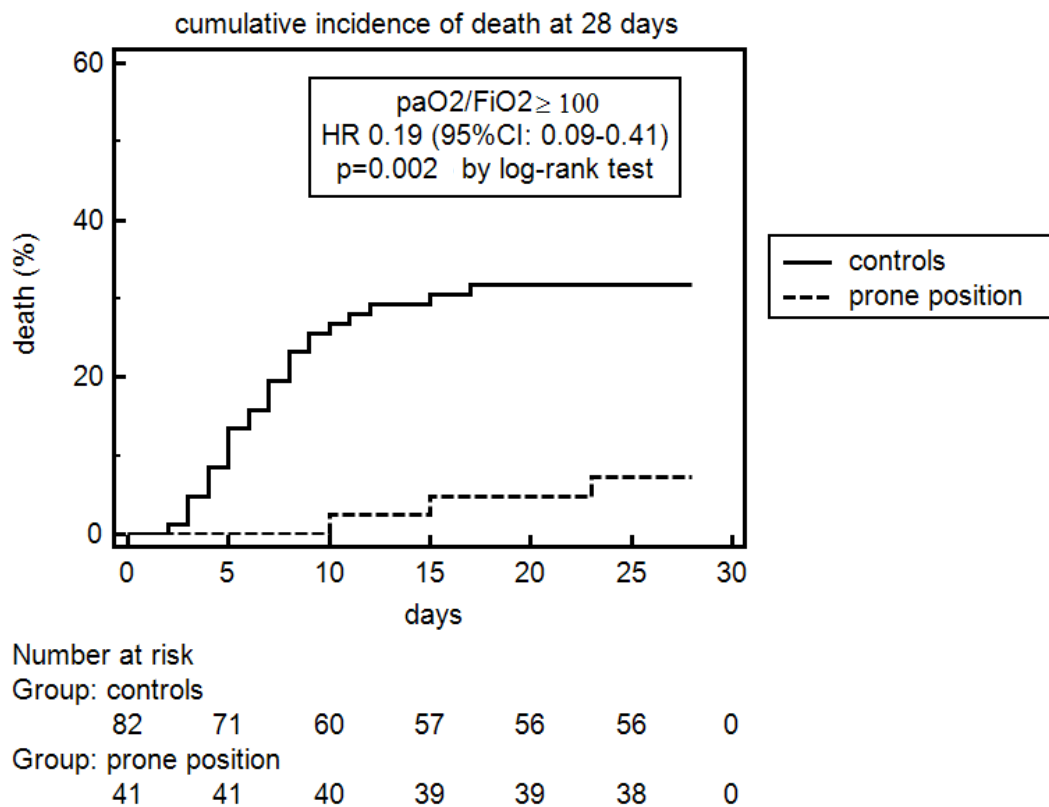
Panel B: NIV failure in patients with $\text{paO}_2/\text{FiO}_2 \geq 100$



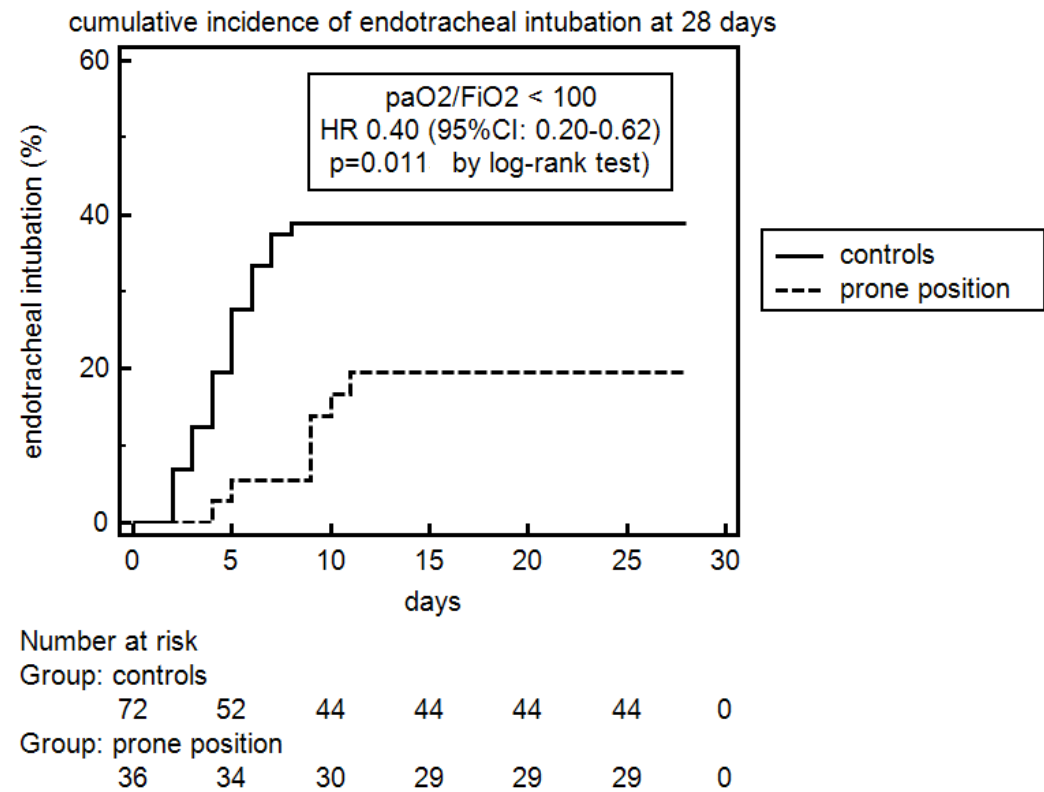
Panel C: death in patients with $\text{paO}_2/\text{FiO}_2 < 100$



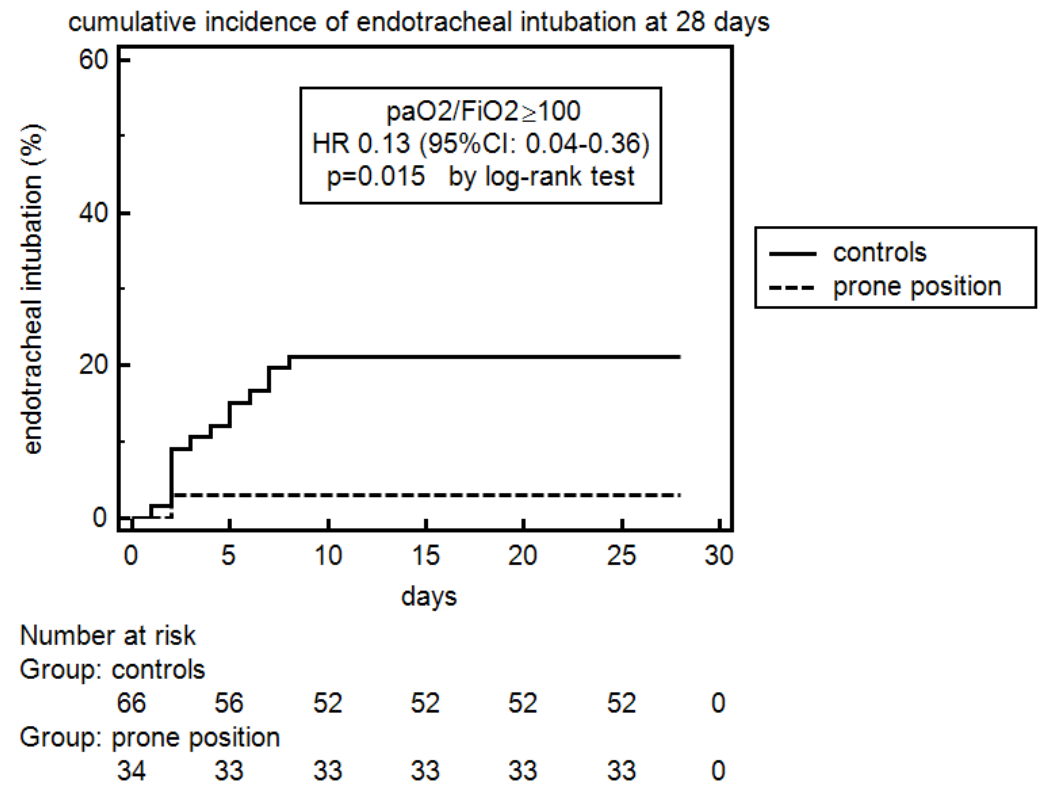
Panel D: death in patients with $\text{paO}_2/\text{FiO}_2 \geq 100$



Panel E: endotracheal intubation in patients with $paO_2/FiO_2 < 100$

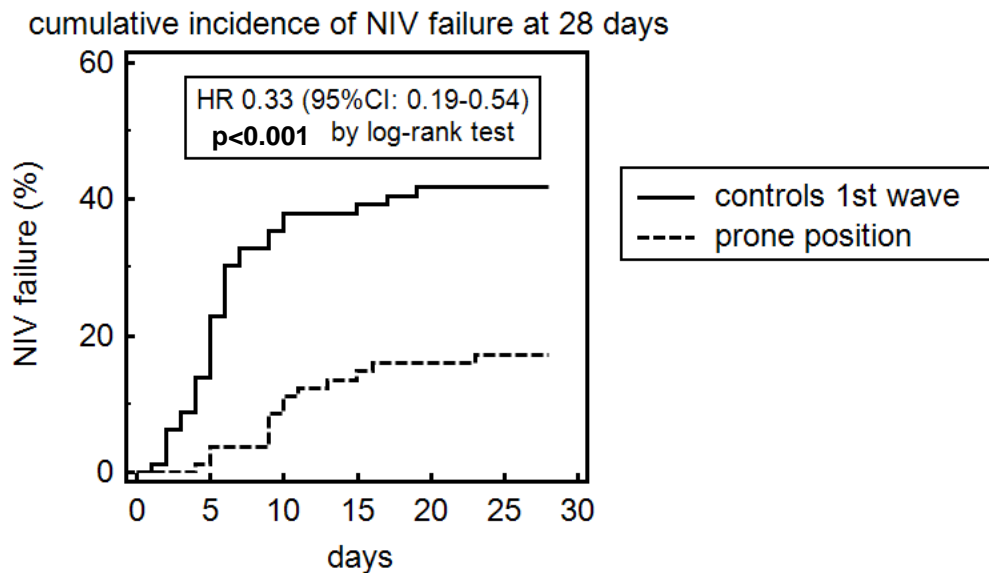


Panel F: endotracheal intubation in patients with $paO_2/FiO_2 \geq 100$



Supplementary Figure 5. NIV failure, death and endotracheal intubation in the prone position group vs. controls enrolled the 1st pandemic wave (March 1st-June 30th, 2020) or the 2nd pandemic wave (July 1st-Dec 15th, 2020).

Panel A: NIV failure (controls from the 1st wave)



Number at risk

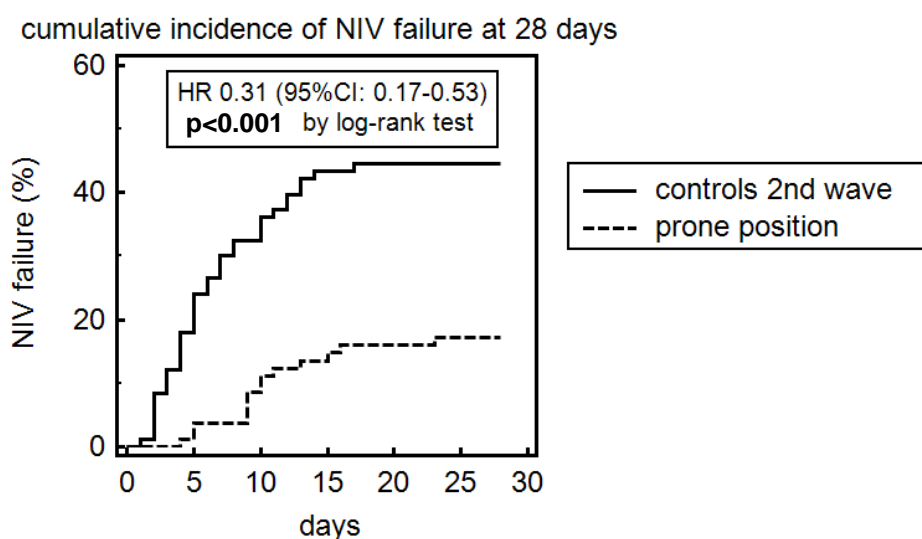
Group: controls 1st wave

79 61 49 48 46 46 0

Group: prone position

81 78 72 69 68 67 0

Panel B: NIV failure (controls from the 2nd wave)



Number at risk

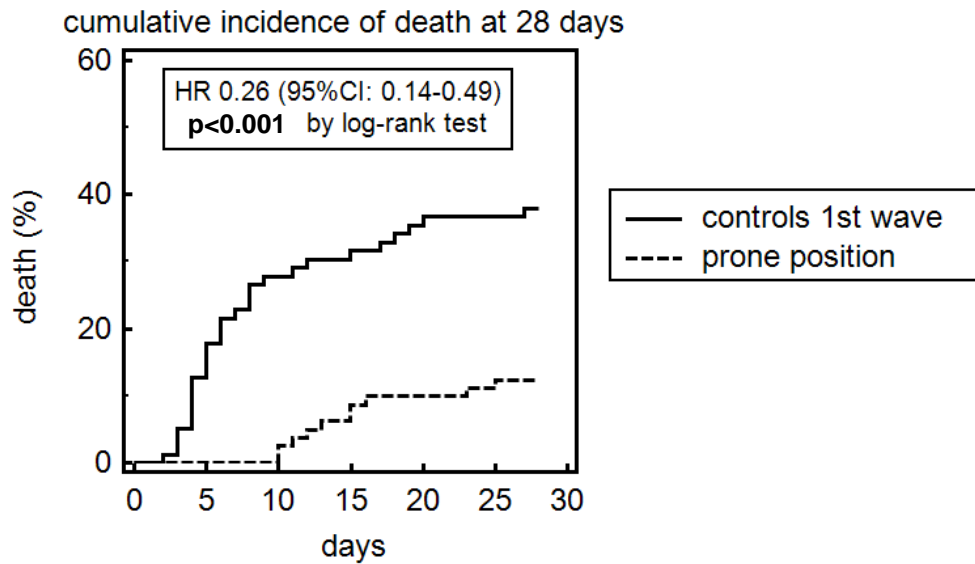
Group: controls 2nd wave

83 63 53 47 46 46 0

Group: prone position

81 78 72 69 68 67 0

Panel C: death (controls from the 1st wave)



Number at risk

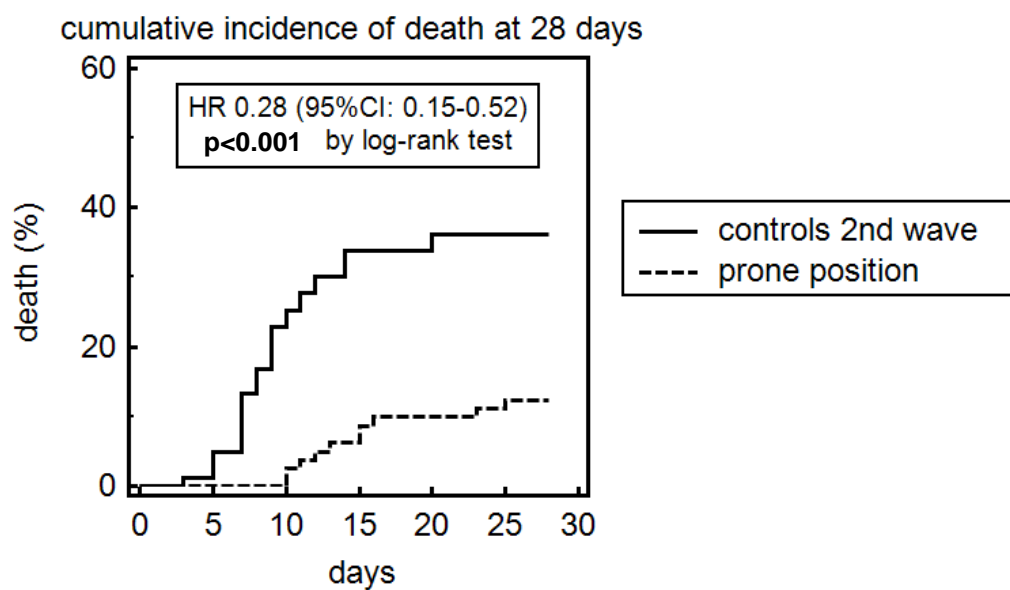
Group: controls 1st wave

79 65 57 54 50 50 0

Group: prone position

81 81 79 74 73 71 0

Panel D: death (controls from the 2nd wave)



Number at risk

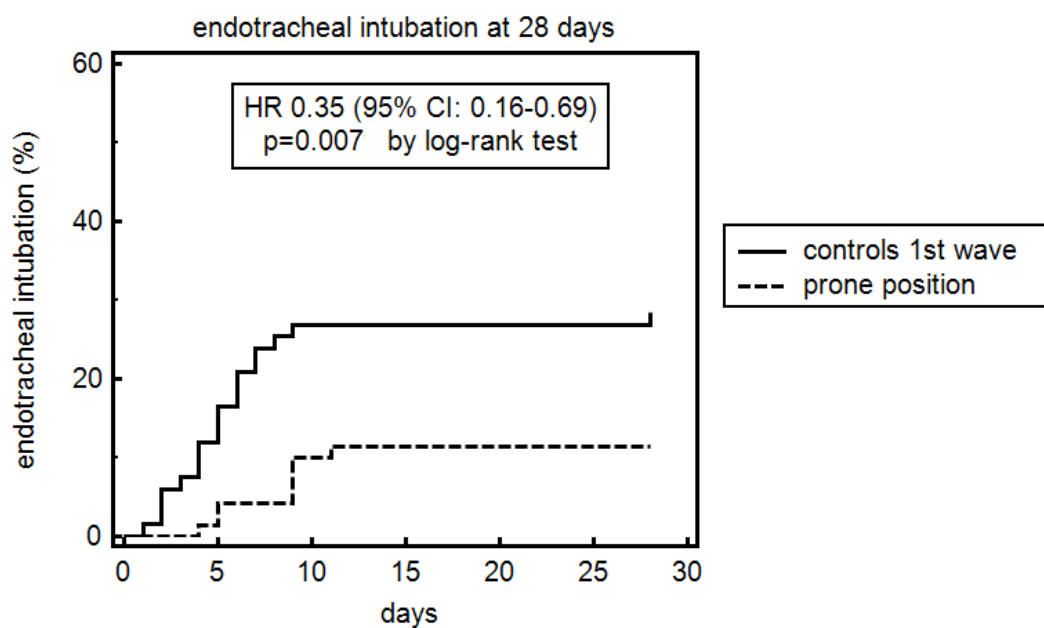
Group: controls 2nd wave

83 79 62 55 53 53 0

Group: prone position

81 81 79 74 73 71 0

Panel E: endotracheal intubation (controls from the 1st wave)



Number at risk

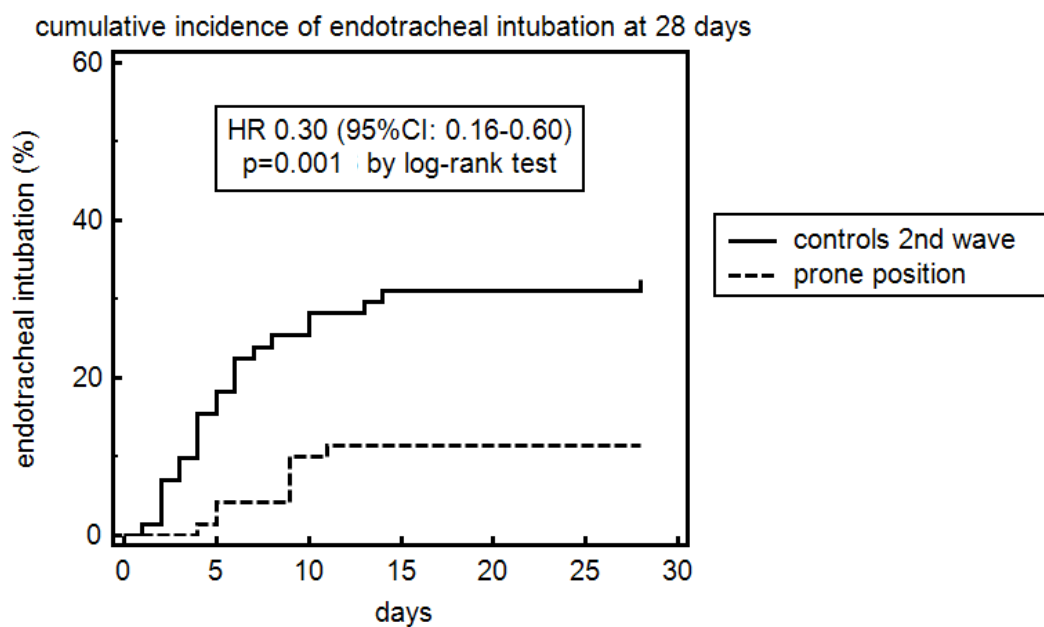
Group: controls 1st wave

67 56 49 49 49 49 0

Group: prone position

70 67 63 62 62 62 0

Panel F: endotracheal intubation (controls from the 2nd wave)



Number at risk

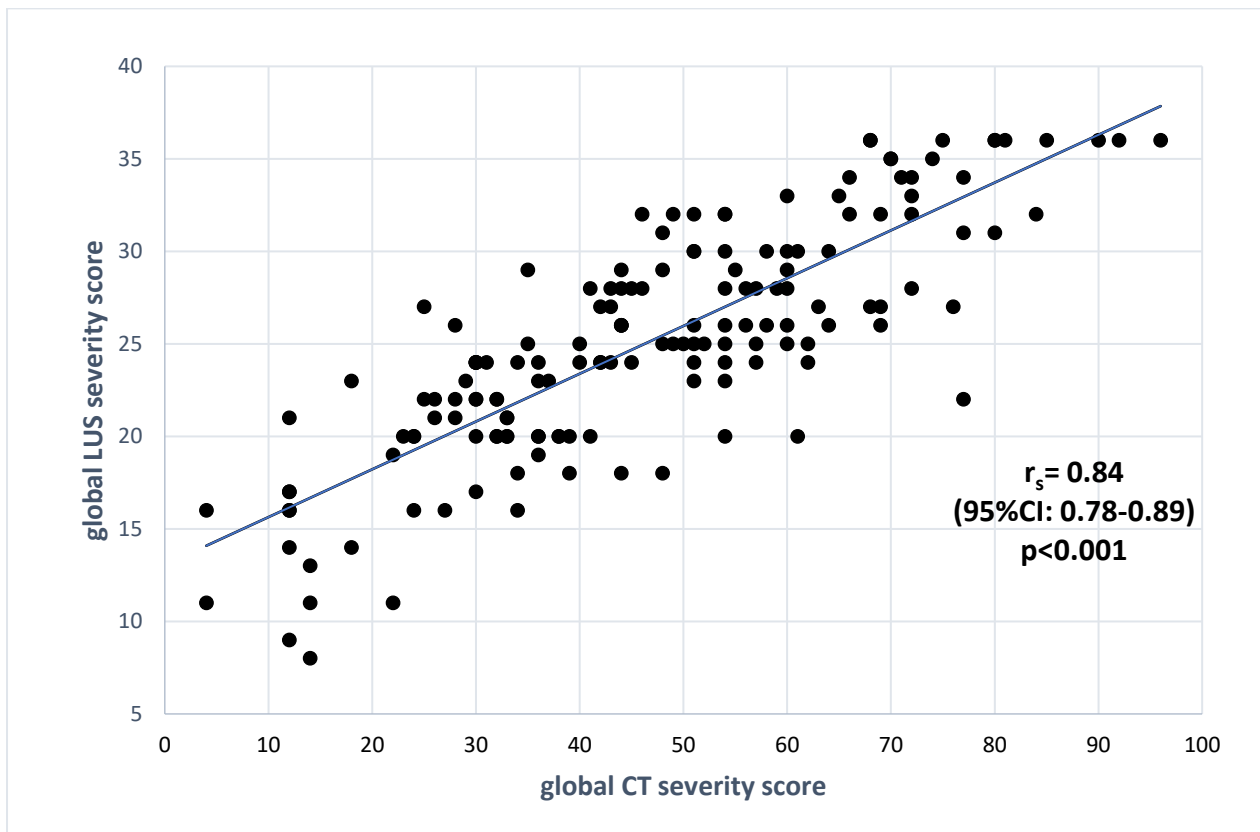
Group: controls 2nd wave

71 58 51 49 49 49 0

Group: prone position

70 67 63 62 62 62 0

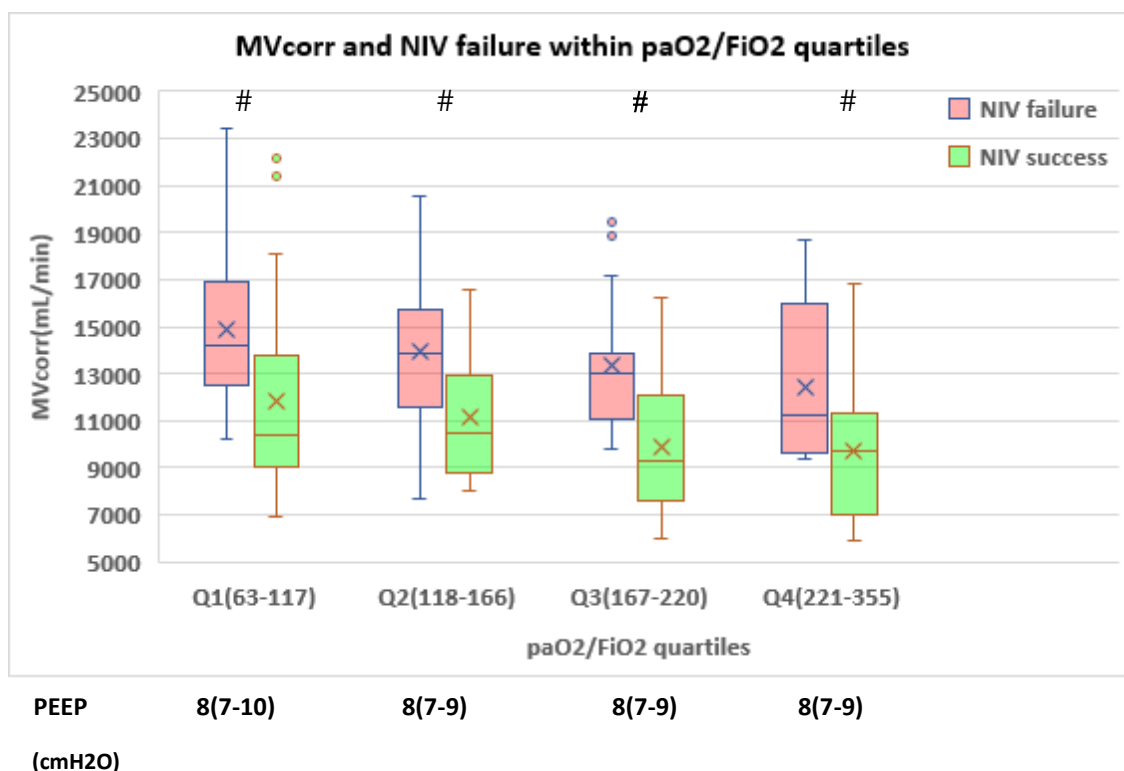
Supplementary Figure 6: correlation between global lung ultrasound (LUS) score and global chest computed tomography (CT) severity score, as proposed by Salaffi et al. in 162 patients with SARS-CoV-2-related acute hypoxemic respiratory failure admitted to the Subintensive Care Unit. The median (IQR) CT severity score was 46(32, 60) and the median (IQR) LUS severity score was 25(21, 30). The Spearman correlation coefficient (r_s) with its 95%CI and statistical significance are shown in the Figure.



Supplementary Figure 7. Relationship between dead space index corrected Minute Ventilation (MVcorr)] and NIV failure, death and ETI within each paO2/FiO2 quartile at timepoint sp1 (i.e. supine position at day 1, corresponding in the PP group to respiration after the first 8-hr overnight PP session)(n=182). paO2/FiO2 range within each quartile and PEEP (median, IQR) at which measurements were made are reported at the bottom of the panels.

* P<0.05 vs. treatment failure within quartile # P<0.001 vs. controls

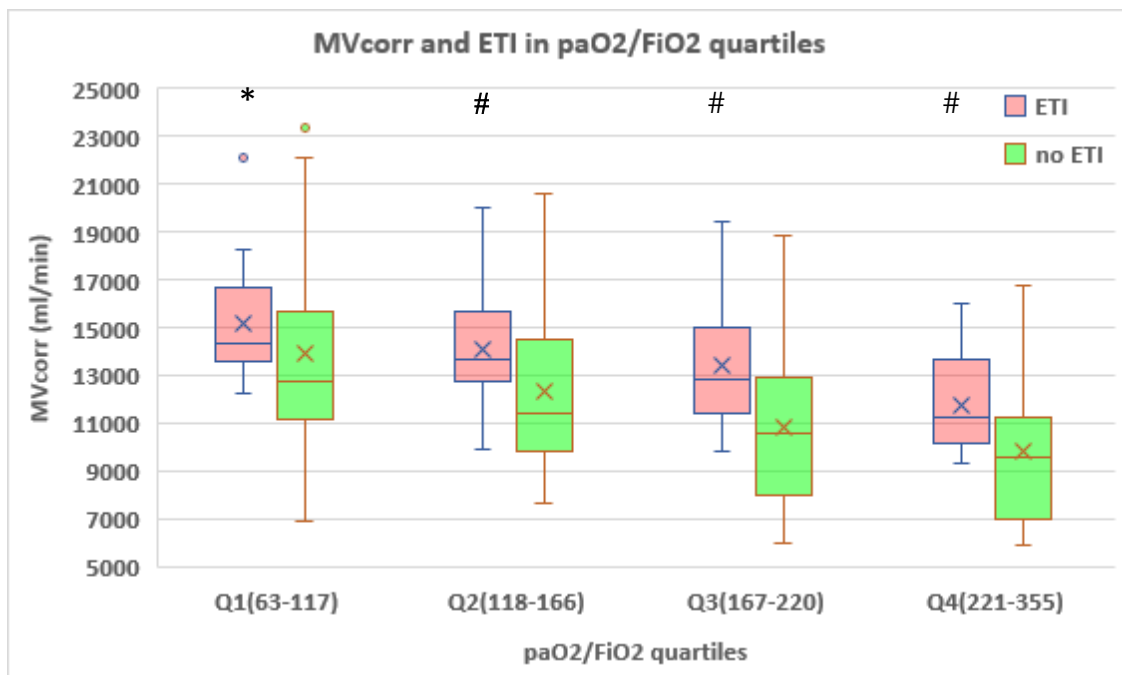
Panel A: MVcorr and NIV failure



Panel B: MVcorr and death



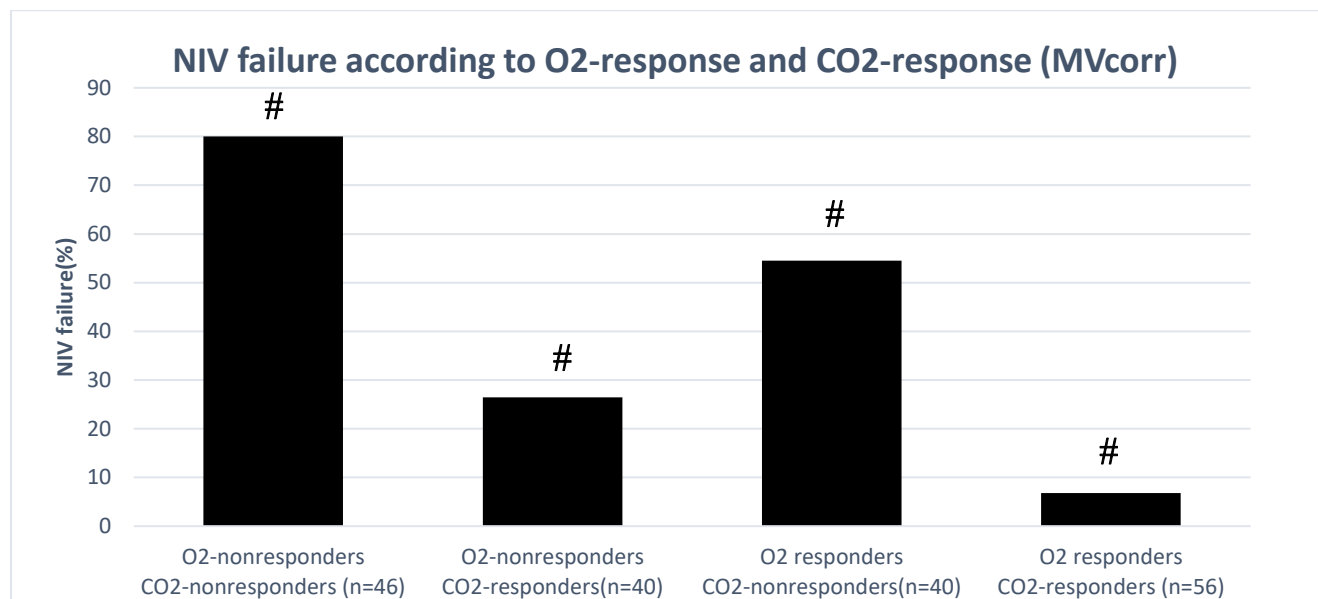
Panel C; MVcorr and ETI



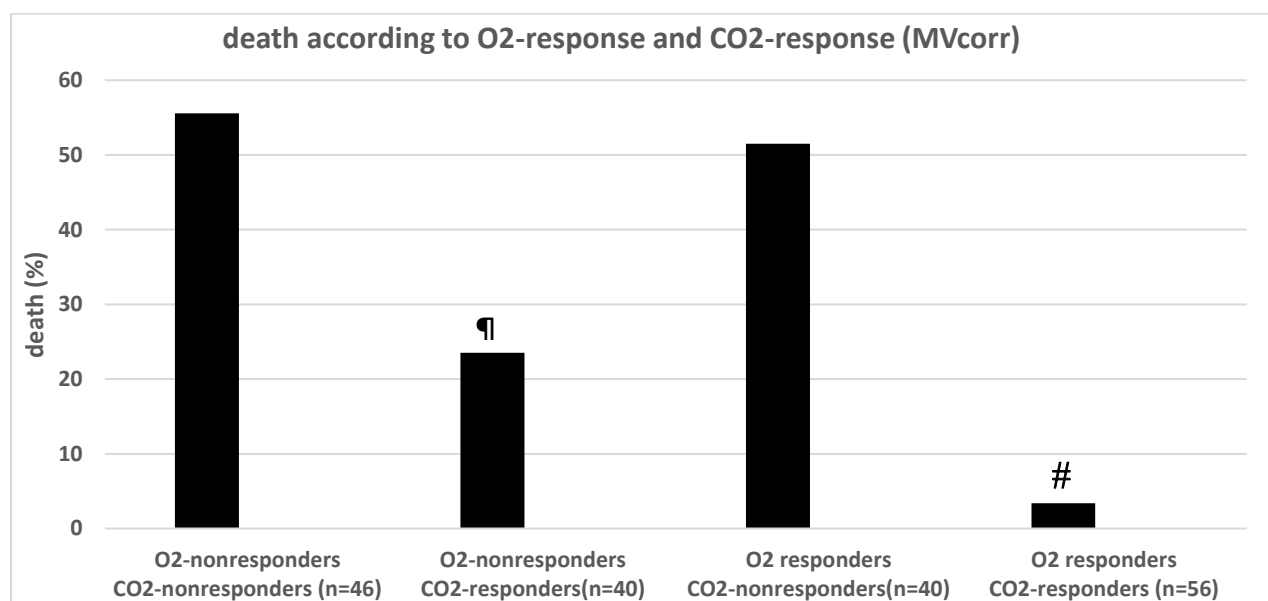
Supplementary Figure 8. Impact of O₂-response and CO₂-response on NIV failure, death and ETL. CO₂-response was assessed via corrected Minute Ventilation(MVcorr).

P<0.01 vs. other groups ¶ P<0.001 vs. other groups

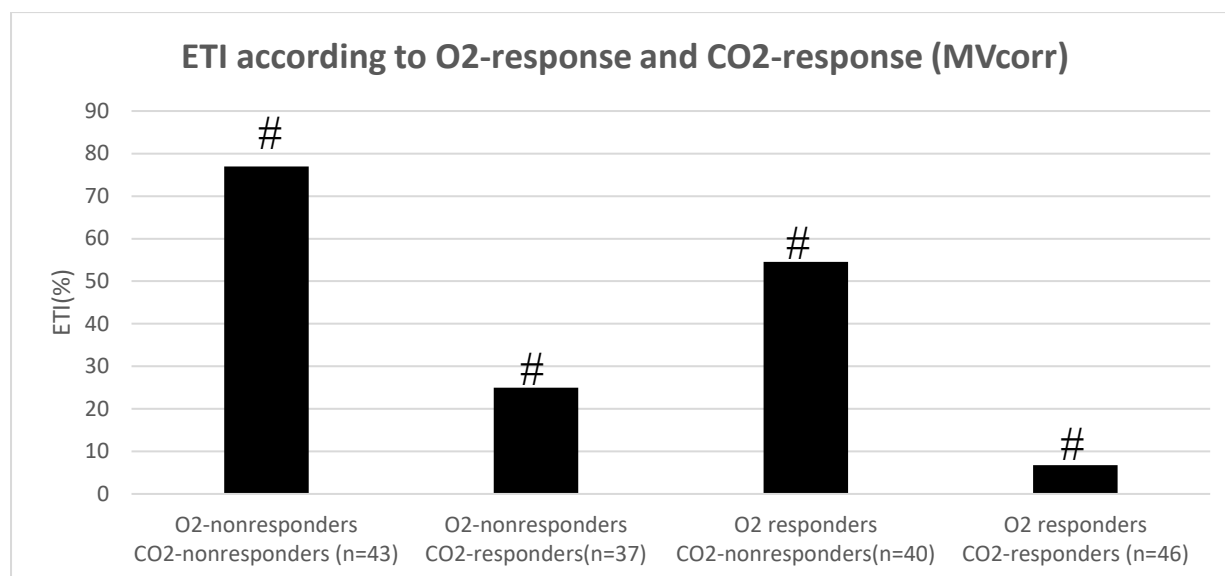
Panel A



Panel B



Panel C



Supplementary Figure 9: serum procalcitonin in PP group and controls after excluding patients with documented (either at admission or after admission to Subintensive Care Unit) bacterial or mycotic infection (n=223)

P<0.001 vs. controls

